

Title: RATIONAL EVOLUTION OF CYTOKINES FOR HIGHER STABILITY,
THE CYTOKINES AND ENCODING NUCLEIC ACID MOLECULES
Applicants: Rene Gantier, et. al Attorney Docket No. 17109-012001/922
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Cytokine regions susceptible to protease attack identified by structural alignment with Lead mutants

of IFN α -2b

IFN- α 2b

CDLPQTHSLGSRRTIMLLAQMRKISLFSCLKDRHDFGFPQEEFGNQFQKAETIPVLHEMIQQIFNLFSFKDSSAAWDETLLDKFYTELYQQQLNDLEACVIOG

VGVTTETPLMKEDSILAVRKYFQRITLYLKEKKYSPCAWEVVRAEIMRSFSLSTNLQESLSRKE

Exemplary protein of the interferons/interleukin-10 family

IFN- β

MSYNLLGFLQRSNFQCKLLWQLNGRLEYCLKDRWNFDIPEEIKQLQQFQKEDAAITIEMLQNIPAIIPRODSSSTGWNETIVENLLANVYHQINHLKTVLEEK

LEKEDPTRGKLMSSHLKRYYGRILHYLKAKEYSHCAWTIVRVEILRNFFYNRLTGVLRN

Exemplary protein of the short-chain cytokines family

EPO

APPRLICDSRVLERLYLLEAKEAENITTCGAEHCSLNENITVPDTKYNFYAKRMEVGQAAVEVWQGLALLSEAVLRGQALLVNSSQPWEPLQLHVDKAVSGLRSL

TTLLRALGAQKEAISNSDAASAAPLRTITADTFRKLFRVYSNFLRGKCLKLYTGEACRTGDR

Exemplary protein of the long-chain cytokines family

G-CSF

TPLGPASSLPQSFLLKCLEQVRKIQGDGAALQEKLVSECATYKLCHEELVLLGHSIGIPWAPLSSCPSPQALQAGCLSQLHSGFLFYQGLLQALEGISPELGPTLDTLQL

DVADFAATTIWOQMEELGMAPALQPTQGAMPAFASAFORRAGGVLVASHLQSFLEVSRYRVLRLHAQP

FIG. 9